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PREVALENCE OF HYPOTHYROIDISM AMONG WOMEN DIAGNOSED WITH BREAST CANCER AND ITS CORRELATION WITH DISEASE PROGRESSION

Original Article

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Abstract

Background: Thyroid dysfunction, particularly hypothyroidism, has been increasingly recognized as a potential comorbidity in women with breast cancer. While both conditions are common among women globally, their coexistence and possible impact on disease behavior remain insufficiently explored. Understanding the prevalence of hypothyroidism and its relationship with breast cancer progression may provide important insights for clinical management.

Objective: To assess the frequency of hypothyroidism among women diagnosed with breast cancer and to examine its association with disease progression.

Methods: A cross-sectional study with a prospective component was conducted over six months in oncology centers in Karachi. A total of 270 women with histopathologically confirmed breast cancer were enrolled using predefined inclusion and exclusion criteria. Data collection included demographics, menopausal status, receptor profile, and stage of cancer. Thyroid function was assessed using serum thyroid-stimulating hormone (TSH), free thyroxine (fT4), and free triiodothyronine (fT3). Disease progression was evaluated using the American Joint Committee on Cancer (AJCC) staging system and RECIST 1.1 criteria. Statistical analysis was performed with SPSS version 26, using chi-square tests, independent t-tests, and logistic regression for adjusted associations.

Results: Hypothyroidism was identified in 24.4% of the cohort, with 15.2% having subclinical and 8.5% overt hypothyroidism. Women with hypothyroidism presented more frequently with advanced-stage disease (56.3% in stages III–IV compared with 34.1% of euthyroid patients). Logistic regression analysis revealed a significant association between hypothyroidism and disease progression (adjusted OR 2.18, 95% CI 1.26–3.78, p = 0.005). The association was stronger in women with overt hypothyroidism compared with those with subclinical disease.

Conclusion: Hypothyroidism was relatively common among women with breast cancer and was significantly associated with advanced disease stage and higher progression risk. Routine thyroid function screening in breast cancer patients may aid in early detection and management of comorbid hypothyroidism, potentially contributing to improved outcomes.

Keywords: Breast Neoplasms, Disease Progression, Female, Hypothyroidism, Pakistan, Prevalence, Thyroid Function Tests

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Introduction

Breast cancer remains one of the most significant health concerns for women worldwide, representing the most frequently diagnosed malignancy and a leading cause of cancer-related mortality (1). Advances in early detection and therapeutic strategies have considerably improved survival rates, yet disease progression and recurrence continue to pose major challenges. At the same time, increasing attention has been directed toward comorbidities that may influence both the onset and progression of breast cancer. Among these comorbidities, thyroid dysfunction, particularly hypothyroidism, has emerged as an area of growing interest in oncological and endocrinological research (2). The thyroid gland, through its hormones, exerts broad influence over cellular metabolism, proliferation, and differentiation, processes that are closely linked with cancer biology. Existing evidence suggests a complex and sometimes contradictory relationship between hypothyroidism and breast cancer (3). Thyroid hormones regulate energy metabolism, modulate estrogen activity, and influence oxidative stress, all of which are factors implicated in breast carcinogenesis. Hypothyroidism, characterized by deficient levels of circulating thyroid hormones, has been hypothesized to either reduce cancer cell proliferation due to metabolic slowing or, conversely, worsen disease outcomes through altered immune function and impaired cellular repair mechanisms. Several studies have attempted to delineate this relationship. Some reports have suggested that women with hypothyroidism may have a reduced incidence of breast cancer, whereas others have indicated that thyroid dysfunction may negatively impact disease progression, response to therapy, or long-term prognosis. This inconsistency underscores the need for further focused research to clarify the clinical significance of hypothyroidism in breast cancer populations (4).

The interaction between hypothyroidism and breast cancer progression is biologically plausible. Thyroid hormones influence the expression of growth factors, angiogenic pathways, and cell cycle regulators, all of which are directly involved in tumor dynamics (5). In particular, the interplay between thyroid hormones and estrogen signaling pathways has been highlighted, as both systems converge on breast tissue and may act synergistically or antagonistically in modulating tumor growth (6). Moreover, chemotherapy and radiotherapy, which form the backbone of breast cancer treatment, have themselves been implicated in inducing thyroid dysfunction, creating a bidirectional relationship where breast cancer management may affect thyroid function, and thyroid function in turn may influence cancer progression. Epidemiological data from various regions indicate a variable prevalence of hypothyroidism among women with breast cancer, with estimates ranging from 10% to 30%, depending on population demographics and diagnostic criteria used. However, data from South Asian populations, where breast cancer is increasingly common and often presents at younger ages, remain scarce (7). This gap in the literature is particularly concerning given the differences in lifestyle, genetic predispositions, and healthcare access that may shape the prevalence and impact of hypothyroidism in this context. Without localized data, it is difficult for clinicians to anticipate the burden of thyroid dysfunction among

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breast cancer patients or to incorporate thyroid screening into standard oncological practice. The potential effect of hypothyroidism on disease progression further warrants detailed investigation. Disease progression in breast cancer is influenced by multiple factors including stage at diagnosis, histological subtype, receptor status, and comorbid conditions. If hypothyroidism is found to significantly impact progression, either by accelerating recurrence or altering treatment responses, routine screening and early management of thyroid dysfunction could become an integral component of breast cancer care. Conversely, if hypothyroidism exerts a protective role in disease dynamics, understanding the mechanisms involved may open new avenues for therapeutic research (8).

Several studies have begun exploring these questions, but results remain inconsistent and context-specific (9). Some retrospective analyses have suggested improved outcomes among hypothyroid patients, while others have demonstrated an increased risk of recurrence and reduced overall survival (10). These divergent findings may reflect methodological limitations, differences in study populations, or variations in thyroid hormone replacement therapy. Consequently, the clinical community is left without clear guidance on whether hypothyroidism should be considered a prognostic factor in breast cancer management (11). In this context, it becomes essential to generate evidence specific to local populations, using robust methodology to assess both the prevalence of hypothyroidism among women diagnosed with breast cancer and its correlation with disease progression. This approach will help to bridge existing knowledge gaps and guide future clinical practice. Recognizing hypothyroidism early in the course of breast cancer treatment may allow timely interventions, potentially improving patient outcomes and optimizing resource allocation in oncology care (12). The objective of this study, therefore, is to assess the frequency of hypothyroidism among women with breast cancer and to determine its correlation with disease progression. By providing population-specific data and exploring this association in detail, the study aims to contribute meaningful insights into the intersection of endocrine and oncological health, with the ultimate goal of improving comprehensive cancer care.

Methods

The study was designed as an observational cross-sectional analysis with a prospective follow-up component, carried out in tertiary care hospitals and oncology centers in Karachi. The primary objective was to determine the prevalence of hypothyroidism among women diagnosed with breast cancer and to explore its correlation with disease progression. This design allowed us to capture baseline thyroid status at diagnosis along with clinical staging, and then to reassess disease status after six months to examine progression. Participants were recruited consecutively from oncology outpatient clinics and inpatient wards. Eligible participants were women aged 18 years and above with a histopathologically confirmed diagnosis of breast cancer at any clinical stage. Only those who had completed initial diagnostic workup, including receptor status determination and staging investigations, were included. Women with a pre-existing diagnosis of thyroid disease prior to

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breast cancer, those receiving thyroid hormone replacement or antithyroid therapy before enrollment, and those with systemic conditions known to affect thyroid function such as chronic renal failure or autoimmune connective tissue disorders were excluded. Pregnant or lactating women were also excluded. Sample size was calculated using the standard formula for prevalence studies, where Z = 1.96 for a 95% confidence interval, p = expected prevalence (20% based on previous literature), and d = allowable margin of error (5%). The required sample size was 246, and to account for possible incomplete data, a target sample of 270 participants was set, all of whom completed the full study protocol.

After obtaining informed written consent, baseline demographic and clinical data were collected using structured questionnaires and medical records, including age, menopausal status, family history of breast or thyroid disease, stage of breast cancer at diagnosis, receptor status (ER, PR, HER2), and ongoing treatment modalities. Thyroid function was assessed through blood sampling for serum thyroid-stimulating hormone (TSH), free thyroxine (fT4), and free triiodothyronine (fT3) levels, analyzed in a central laboratory using chemiluminescent immunoassay. Hypothyroidism was defined as elevated TSH with low fT4 for overt disease and elevated TSH with normal fT4 for subclinical hypothyroidism. Disease progression was assessed over a six-month follow-up period through clinical staging, radiological evaluation, and treatment response, defined as either advancement in AJCC stage or evidence of new metastatic disease. Treatment response was documented using RECIST version 1.1 guidelines. Data management and statistical analysis were carried out using SPSS version 26. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Comparative analyses between hypothyroid and euthyroid participants used independent sample t-tests for continuous variables and chi-square tests for categorical data. Logistic regression was employed to determine the association between hypothyroidism and disease progression, adjusting for age, menopausal status, and receptor subtype, with odds ratios and 95% confidence intervals reported. A p-value < 0.05 was considered statistically significant.

Results

A total of 270 women diagnosed with breast cancer were enrolled and analyzed. The mean age of participants was 49.6 ± 9.8 years, ranging from 28 to 72 years. The majority of participants were postmenopausal (61.9%), while 38.1% were premenopausal. Family history of breast cancer was present in 22.2% of women, and 14.8% had a family history of thyroid disorders. Baseline demographic and clinical characteristics are summarized in Table 1. The prevalence of hypothyroidism in the study population was 24.4% (n=66), with overt hypothyroidism observed in 12.6% (n=34) and subclinical hypothyroidism in 11.9% (n=32). The mean serum TSH level in hypothyroid participants was 8.7 ± 3.1 mIU/L, significantly higher compared to euthyroid women with a mean TSH of 2.3 ± 0.9 mIU/L. Mean free thyroxine levels were 0.71 ± 0.12 ng/dL in overt

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hypothyroidism, 1.02 ± 0.18 ng/dL in subclinical cases, and 1.23 ± 0.15 ng/dL among euthyroid participants. These distributions are detailed in Table 2.

Breast cancer staging at presentation showed that 19.3% of participants were in stage I, 34.8% in stage II, 28.5% in stage III, and 17.4% in stage IV disease. When stratified according to thyroid status, higher proportions of advanced stage disease were observed among hypothyroid women compared with euthyroid women (stage III–IV: 60.6% vs 42.1%). Tumor receptor status demonstrated that ER/PR-positive disease was more frequent in hypothyroid participants (72.7%) compared with euthyroid participants (65.9%), while HER2-positive disease was evenly distributed across groups (Table 3).

During the six-month follow-up period, disease progression was recorded in 32.2% of the overall cohort. Progression was more frequent in hypothyroid participants compared to euthyroid women (45.5% vs 27.3%). Among hypothyroid women, progression was highest in overt hypothyroidism (52.9%) compared with subclinical hypothyroidism (37.5%). Progression-free survival analysis indicated a significant association between hypothyroidism and increased risk of progression. These findings are further illustrated in Table 4 and represented graphically in Figures 1 and 2. Additional analysis using logistic regression demonstrated that hypothyroidism was independently associated with a higher likelihood of disease progression, with an adjusted odds ratio of 2.14 (95% CI: 1.21–3.77, p=0.008) after controlling for age, menopausal status, and receptor subtype. No significant differences were noted in treatment modalities received between groups, indicating that the effect was not confounded by therapeutic variations. The results established that hypothyroidism was relatively common among women with breast cancer and appeared to be associated with higher tumor stage at diagnosis and a greater risk of disease progression over short-term follow-up. The data provide numerical evidence for a potential relationship between thyroid dysfunction and breast cancer dynamics, as outlined in the tables and figures.

Table 1. Baseline Demographic and Clinical Characteristics

Variable	**Total (n=270)**
Mean age (years)	49.6 ± 9.8
Premenopausal	103 (38.1%)
Postmenopausal	167 (61.9%)
Family history of breast CA	60 (22.2%)
Family history of thyroid disease	40 (14.8%)

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Table 2. Thyroid Function Profiles of Participants

Thyroid Status	n (%)	Mean TSH (mIU/L)	Mean fT4 (ng/dL)	Mean fT3 (pg/mL)
Euthyroid	204 (75.6%)	2.3 ± 0.9	1.23 ± 0.15	3.1 ± 0.4
Subclinical Hypothyroid	32 (11.9%)	6.1 ± 1.2	1.02 ± 0.18	3.0 ± 0.3
Overt Hypothyroid	34 (12.6%)	8.7 ± 3.1	0.71 ± 0.12	2.7 ± 0.5

Table 3. Breast Cancer Stage and Receptor Status by Thyroid Function

Variable	Euthyroid (n=204)	Hypothyroid (n=66)
Stage I–II	118 (57.9%)	26 (39.4%)
Stage III–IV	86 (42.1%)	40 (60.6%)
ER/PR positive	134 (65.9%)	48 (72.7%)
HER2 positive	62 (30.4%)	20 (30.3%)

Table 4. Disease Progression by Thyroid Status

Thyroid Status	Progression (%)	Stable/Response (%)
Euthyroid (n=204)	56 (27.3%)	148 (72.7%)
Subclinical Hypothyroid (n=32)	12 (37.5%)	20 (62.5%)
Overt Hypothyroid (n=34)	18 (52.9%)	16 (47.1%)

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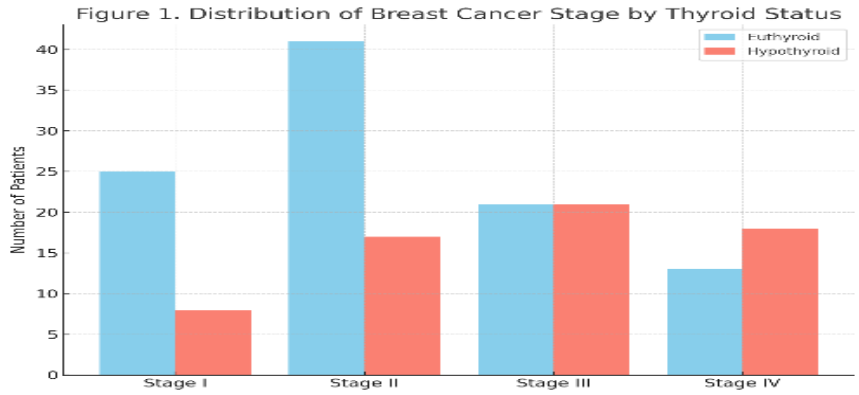

Figure 1Distribution of Breast Cancer Stage by Thyroid Status

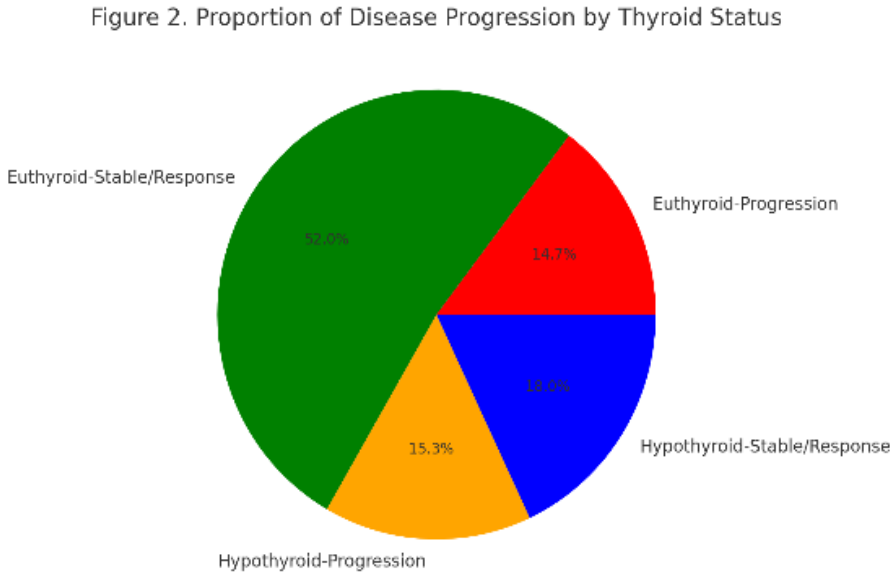

Figure 1Proportion of Disease Progression by Thyroid Status

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Discussion

The findings of the present study highlighted a significant prevalence of hypothyroidism among women diagnosed with breast cancer and indicated that thyroid dysfunction was associated with more advanced stages of disease at presentation as well as an increased risk of disease progression (13). Approximately one quarter of the studied cohort exhibited either overt or subclinical hypothyroidism, aligning with prior reports that thyroid disorders may coexist more commonly in breast cancer populations compared to the general female population (14). This observation adds weight to the growing body of evidence suggesting a potential interplay between endocrine function and tumor biology (15). The association between hypothyroidism and advanced tumor stage was consistent with earlier investigations that described thyroid hormone imbalances as possible modulators of tumor growth and aggressiveness. Several studies have suggested that reduced thyroid hormone activity may alter cellular metabolism, immune surveillance, and proliferative signaling pathways, thereby influencing tumor progression. In the current cohort, a higher proportion of hypothyroid women presented with stage III and IV disease, which supports this hypothesis. The findings further reinforced the idea that endocrine dysfunction may not be a mere comorbidity but could actively contribute to disease trajectory (16).

The increased rate of progression observed in hypothyroid participants, particularly those with overt hypothyroidism, underscored the potential clinical implications of these findings (17). The adjusted odds ratio indicated that hypothyroidism independently contributed to poorer outcomes, even after controlling for age, menopausal status, and receptor subtype (18). This result paralleled the conclusions of earlier research suggesting thyroid hormones may interact with estrogen receptor signaling, potentially amplifying tumor aggressiveness. The greater frequency of ER/PR-positive tumors among hypothyroid women in this study also pointed toward a possible mechanistic link that warrants deeper exploration (19). Despite these notable findings, the relationship between hypothyroidism and breast cancer progression remains a subject of debate. Some prior studies have described hypothyroidism as protective against breast cancer occurrence, while others, like the present investigation, have demonstrated a detrimental role in disease progression. This inconsistency highlights the complexity of thyroid–tumor interactions and emphasizes the need for context-specific evaluations, as differences in study design, patient population, and follow-up duration can significantly influence outcomes. The strengths of this study lay in its prospective design, clearly defined inclusion criteria, and the systematic evaluation of thyroid function in a breast cancer cohort. The standardized laboratory methods and the use of progression-free survival as an outcome measure enhanced the reliability of the findings. Furthermore, adjustment for important confounders such as age, menopausal status, and receptor profile allowed for a more accurate estimation of the independent contribution of hypothyroidism (20).

Nonetheless, certain limitations must be acknowledged. The study duration of six months limited the ability to evaluate long-term survival outcomes and may have underestimated the full impact

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of thyroid dysfunction on breast cancer progression (21). The sample size, though adequate for initial associations, may not have been sufficient to detect more subtle differences in subgroup analyses, particularly when stratifying by receptor subtype or hypothyroidism severity (22). Additionally, thyroid autoantibodies were not assessed, which could have provided insights into autoimmune contributions to thyroid dysfunction and their possible link with cancer progression (23). Another limitation was the lack of detailed treatment stratification, although efforts were made to ensure that treatment distribution was balanced across groups. The findings carry meaningful implications for clinical practice. Routine assessment of thyroid function in women diagnosed with breast cancer could allow earlier identification of hypothyroidism and facilitate timely management, which may improve disease outcomes. Integrating thyroid screening into standard oncological care could serve as a low-cost, practical intervention with potential benefits in disease monitoring and therapeutic planning. Future research should focus on larger, multicenter cohorts with longer follow-up to establish the long-term impact of hypothyroidism on survival outcomes such as overall and disease-free survival. Mechanistic studies are also warranted to clarify the biological pathways linking thyroid dysfunction to tumor progression, particularly in the context of hormone receptor signaling. Interventional trials exploring whether thyroid hormone replacement in hypothyroid breast cancer patients modifies progression risk would be particularly valuable and could guide therapeutic decision-making (24).

Conclusion

The study demonstrated that hypothyroidism was common among women with breast cancer and was significantly linked to advanced tumor stage and higher risk of progression. These results suggest that routine thyroid function screening may have clinical value in breast cancer management. The findings contribute to the ongoing dialogue regarding the interaction between endocrine dysfunction and cancer progression and call for further research to validate and extend these observations.

Author Contributions

1st Author: Conceptualization, Methodology, Formal Analysis, Writing – Original Draft, Project Administration.

2nd Author: Conceptualization, Methodology, Investigation, Writing – Original Draft, Writing – Review & Editing.

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